REMARKS/ARGUMENTS

I. Introduction

Upon entry of the present amendment, claims 12-18 will be pending in this application. Claim 12 has been amended to clarify certain aspects of the invention and claims 13-18 have been added to further define the invention. Support for the amendment and new claims appears in the specification claims as originally filed. No new matter has been added.

Because the present amendments materially reduce the issues for appeal, and place this application into better condition for allowance, entry is appropriate under 37 C.F.R. § 1.116, and is respectfully requested. Based on the following remarks, Applicants respectfully request reconsideration and allowance of the pending claims.

II. 35 U.S.C. § 103

The Examiner has rejected Claim 12 under 35 U.S.C. § 103(a) as being unpatentable over Lee et al (WO 00/15194) in view of Corrigan et al. (WO 99/03451). The Examiner's position is that it would have been obvious for one of skill in the art to use the casein disclosed by Corrigan et al. in conjunction with the calcium phosphate particles disclosed by Lee et al. in order to take advantage of the reduced gastrointestinal irritation and increased drug delivery associated with the use of casein. Applicants respectfully traverse the Examiner's rejection, request that is be reconsidered and withdrawn, and submit that the pending claims should be allowed.

A. The Lee and Corrigan references are not properly combinable

In order to establish a *prima facie* case of obviousness, three criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the references or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art references when combined must teach or suggest all the claim limitations. See MPEP § 2142. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must be found in the prior art, and not based on the applicant's disclosure." The initial burden is on the Examiner to provide some suggestion of the desirability in doing what the inventor has done.

The Examiner admits that the Lee reference does not disclose the use of casein as a coating substance for the calcium phosphate particles. Moreover, nowhere in the Lee reference is there any suggestion of (a) delivering the particles orally or (b) for coating the particles to prevent their degredation by digestive enzymes. Lee discusses encapsulating its calcium phosphate particles in a liposome or polymer, but that is because "liposome and polymers (e.g., PMMA, PLGA, PLA, gelatin, poly(phosphazene)), particularly biodegradable polymers, may also increase adjuvant activity by themselves serving as a delivery vehicle for the inventive calcium phosphate adjuvant." *See* Lee at page 20. Liposome drug delivery is a completely different category of drug delivery from the present invention and completely different from the drug delivery of Corrigan. Liposomes are composed of a phospholipid layer in which the phosphorus moiety is on the outside and the

lipid moiety is on the inside. The layer encapsulates a watery liquid, not solid particles, proteins, or fatty acids. Caseins are phosphorylated proteins but they are not phospholipids.

Moreover, Lee does not disclose or suggest delivering its particles orally. Page 30 of the Lee reference describes a myriad of administration methods, including injection, surgical implantation, transdermal delivery, mucosal delivery, inhalation, and ocular administration. There is no suggestion that the treatment may be delivered orally or that it would be desirable to provide a way for such a delivery. Accordingly, one or ordinary skill in the art would not be motivated to coat the Lee particles with the casein described by the Corrigan reference, which is directed to a way to prevent gastrointestinal irritation due to delivery of drugs that have gastrointestinal irritating effects, to provide for oral delivery of the Lee particles. There is simply no teaching in either reference that suggests such a combination.

B. Even if the references were combinable, the claimed invention would not result

Even if the Lee and Corrigan references were combined, the presently-claimed invention would not result. The Lee particles are different from Applicant's particles, and the Corrigan reference discloses the use of casein in pharmaceutical compositions to reduce the irritating effects of the active ingredient. Corrigan specifically indicates that its invention is for use with active ingredients that have gastrointestinal irritating effects. *See* page 5. Its particles are made by mixing and compression, granulation processes, spray drying of freeze drying the components together. By contrast, Applicants' particles are produced by reconstructing casein micelles around therapeutic agent-loaded CAP particles for the purpose of creating a protective coat surrounding the CAP-therapeutic agent particles. Neither

Corrigan or Lee nor their combination disclose a calcium phosphate core, a therapeutic agent associated with the core; and a layer comprising casein at least partially covering and forming a protective coating that encapsulates the core, as presently claimed. Because the references, alone or in combination, do not teach or suggest each limitation of claims 12-18, Applicants respectfully request reconsideration of the current rejections and reconsideration thereof.

CONCLUSION

For at least the above reasons, Applicant respectfully requests allowance of claims 12-18 and issuance of a patent containing these claims in due course. If there remain any additional issues to be addressed, the Examiner is urged to contact the undersigned attorney at 404.815.6147.

Respectfully submitted,

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